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TRANSMITTAL LETTER TO THE UNITED STATES

ATTORNEY'S DOCKET NUMBER 50761

DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371

U S APPLICATION NO (If known, see 37 CFR 1.5)

INTERNATIONAL APPLICATION NO
PCT/EP00/09023

INTERNATIONAL FILING DATE
15 September 2000

PRIORITY DATE CLAIMED
28 September 1999

TITLE OF INVENTION: BENZODIAZEPINE DERIVATIVES, THE PREPARATION AND USE THEREOF

APPLICANT(S) FOR DO/EO/US Wilfried LUBISCH, Michael KOCK, Thomas HOEGGER, Roland GRANDEL, Reinhold MUELLER,
Sabine SCHULT

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information

1. /X/ This is a FIRST submission of items concerning a filing under 35 U.S.C. 371
2. / / This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371
3. /X/ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1)
4. /x / A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date
5. /X/ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
 - a. /X/ is transmitted herewith (required only if not transmitted by the International Bureau)
 - b. / / has been transmitted by the International Bureau.
 - c. / / is not required, as the application was filed in the United States Receiving Office (RO/USO)
6. /X/ A translation of the International Application into English (35 U.S.C. 371(c)(2))
7. / / Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
 - a. / / are transmitted herewith (required only if not transmitted by the International Bureau)
 - b. / / have been transmitted by the International Bureau
 - c. / / have not been made, however, the time limit for making such amendments has NOT expired
 - d. / / have not been made and will not be made
8. / / A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. / / An oath or declaration of the inventor(s) (35 U.S.C. 171(c)(4))
10. / / A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5))
- Items 11. to 16. below concern other document(s) or information included
11. / / An Information Disclosure Statement under 37 CFR 1.97 and 1.98
12. / / An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. /X / A FIRST preliminary amendment.
/ / A SECOND or SUBSEQUENT preliminary amendment
14. / / A substitute specification
15. / / A change of power of attorney and/or address letter.
16. /x / Other items or information
International Search Report
International Preliminary Examination Report

U S. Appln. No. (If Known) INTERNATIONAL APPLN NO.
PCT/EP00/09023

ATTORNEY'S DOCKET NO
50761

		CALCULATIONS	PTO USE ONLY
17. /X/ The following fees are submitted			
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):			
Search Report has been prepared by the			
EPO or JPO.....	\$890.00	890.00	
International preliminary examination fee paid to USPTO			
(37 CFR 1.482).....	\$710.00		
No international preliminary examination fee paid to			
USPTO (37 CFR 1.482) but international search fee paid			
to USPTO (37 CFR 1.445(a)(2))..... \$740.00			
Neither international preliminary examination fee			
(37 CFR 1.482) nor international search fee			
(37 CFR 1.445(a)(2)) paid to USPTO \$1,040.00			
International preliminary examination fee paid to			
USPTO (37 CFR 1.482) and all claims satisfied pro			
-visions of PCT Article 33(2)-(4)..... \$100.00			
ENTER APPROPRIATE BASIC FEE AMOUNT = \$		890.00	
Surcharge of \$130.00 for furnishing the oath or declaration			
later than // 20 // 30 months from the earliest			
claimed priority date (37 CFR 1.492(e)).			
Claims	Number Filed	Number Extra	Rate
Total Claims	26 -20	6	X\$18. 108.00
Indep. Claims	3 -3		X\$84.
Multiple dependent claim(s) (if applicable)			+280
TOTAL OF ABOVE CALCULATION		=	998.
Reduction of 1/2 for filing by small entity, if applicable.			
Verified Small Entity statement must also be filed			
(Note 37 CFR 1.9, 1.27, 1.28).			
SUBTOTAL		=	998
Processing fee of \$130. for furnishing the English			
translation later than // 20 // 30 months from the			
earliest claimed priority date (37 CFR 1.492(f)). +			
TOTAL NATIONAL FEE		=	998.
Fee for recording the enclosed assignment (37 CFR 1.21(h))			
The assignment must be accompanied by an appropriate cover			
sheet (37 CFR 3.28, 3.31) \$40.00 per property =			
TOTAL FEES ENCLOSED		=	\$ 998.00
		Amount to be	
		refunded: \$	
		Charged \$	

- a./X/ A check in the amount of \$ 998.00 to cover the above fees is enclosed
- b./ / Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed
- c./X/ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 11-0345. A duplicate copy of this sheet is enclosed

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
KEIL & WEINKAUF
1101 Connecticut Ave., N.W.
Washington, D. C. 20036

Herbert B. Keil
SIGNATURE

Herbert B. Keil
NAME
Registration No. 18,967

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of)
LUBISCH et al.) BOX PCT
)
International Application)
PCT/EP 00/09023)
)
Filed: September 16, 2000)
)

For: BENZODIAZEPINE DERIVATIVES, THE PREPARATION AND USE THEREOF

PRELIMINARY AMENDMENT

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

Prior to examination, kindly amend the above-identified application as follows:

IN THE CLAIMS

Kindly amend the claims as shown on the attached sheets.

R E M A R K S

The claims have been amended to eliminate multiple dependency and to place them in better form for U.S. filing. No new matter is included.

A clean copy of the claims is attached.

Favorable action is solicited.

Respectfully submitted,

KEIL & WEINKAUF



Herbert B. Keil
Reg. No. 18,967

1101 Connecticut Ave., N.W.
Washington, D.C. 20036

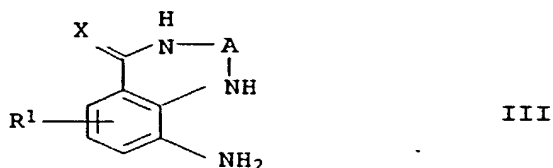
(202)659-0100

CLEAN VERSION OF AMENDED CLAIMS - OZ 50761

3. A compound of the formula I as claimed in claim 1, in which
 - B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.
6. A compound of the formula I as claimed in claim 1, in which B is L_v-Y-M_w , where
 - v is 0, and
 - w is 1, and
 - Y is a bond, and
 - M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and
 - R^1 is hydrogen, and
 - R^4 is $D_{0,1}-F^1_{0,1}-G^1-G^2-G^3$, with G^3 equal to hydrogen, and
 - D is O and NR^{43} , where R^{43} is hydrogen and C_1 - C_3 -alkyl and
 - F^1 is C_2 - C_4 -alkyl.
7. A drug comprising one or more compounds of the formula I as claimed in claim 1 in addition to conventional carriers and excipients.

CLEAN VERSION OF AMENDED CLAIMS - OZ 50761

8. The use of compounds of the formula I as claimed in claim 1 or of the formula I where R^1 , X^1 and A have the meaning as above, and B can be hydrogen and a C_1 - C_6 -alkyl chain, for producing drugs with a PARP-inhibiting effect.
24. A compound of the formula III



in which

A is a C_1 - C_3 chain it being possible for each carbon atom also to carry one or two of the following substituents: C_1 - C_4 -alkyl, OH, O- C_1 - C_4 -alkyl, CO_2H , CO_2 - C_1 - C_4 -alkyl and phenyl or one C atom may also carry an =O group, and

X^1 and R^1 have the meanings stated in claim 1,

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,

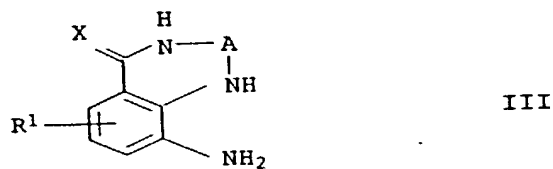
6,8-diamino-2,4-(1H,3H)-quinazolinedione,

8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

MARKED VERSION OF AMENDED CLAIMS - OZ 50761

7. A drug comprising one or more compounds of the formula I as claimed in claim 1 [any of claims 1 to 6] in addition to conventional carriers and excipients.
8. The use of compounds of the formula I as claimed in claim 1 [any of claims 1 to 6] or of the formula I where R¹, X¹ and A have the meaning as above, and B can be hydrogen and a C₁-C₆-alkyl chain, for producing drugs with a PARP-inhibiting effect.
24. A compound of the formula III



in which

A is a C₁-C₃ chain it being possible for each carbon atom also to carry one or two of the following substituents: C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, CO₂H, Co₂-C₁-C₄-alkyl and phenyl or one C atom may also carry an =O group, and

X¹ and R¹ have the meanings stated in claim 1 [the previous claims],

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

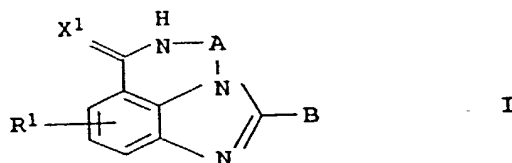
9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,

8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

CLAIMS AS FILED - OZ 50761

1. A compound of the formula I



in which

- A can be a C₁-C₃ chain where each carbon atom may also carry one or two of the following substituents:
 C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, COOH, COO-C₁-C₄-alkyl and phenyl or
 one C atom may also carry an =O group, and
- X¹ can be S, O and NH, and
- R¹ is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C₁-C₆-alkyl, OH, nitro CF₃, CN, NR¹¹R¹², NH-CO-R¹³, O-C₁-C₄-alkyl, where R¹¹ and R¹² are, independently of one another, hydrogen, or C₁-C₄-alkyl, and R¹³ is hydrogen, C₁-C₄-alkyl, C₁-C₄-alkyl-phenyl or phenyl, and
- B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by one R⁴ and a maximum of 3 different or identical R⁵ radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is a radical L_v-Y-M_w in which
- L can be a straight-chain or branched, saturated or unsaturated carbon chain of 1

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to 8 C atoms, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and

M has, independently of L, the same meaning as L, and

Y is a bond, or can be S, O or NR^3 , where R^3 can be hydrogen, branched and unbranched C_1 - C_6 -alkyl, C_1 - C_4 -alkyl-phenyl, phenyl, and

v can be 0 and 1, and

w can be 0 and 1, and

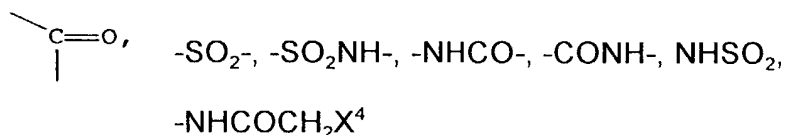
when Y is a bond, R^4 and R^5 are not both hydrogen, and

when B is L_v -Y- M_w , R^1 is not chlorine or NO_2 and

R^4 is hydrogen and $-(D)_p$ -(E)_s-(F¹)_q-G¹-(F²)_r-(G²)-G³, where

D can be S, NR^{43} and O

E can be phenyl,



and

X^4 can be S, O or NH, and

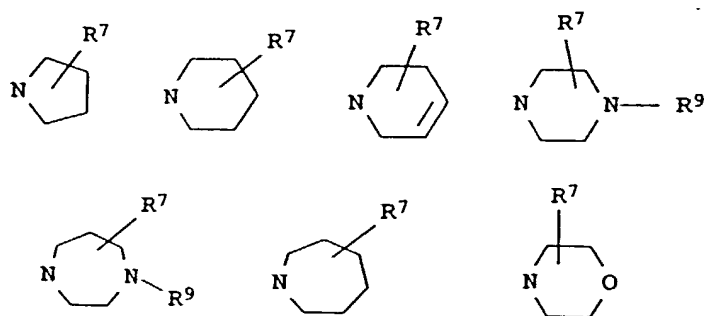
F¹ can be a straight-chain or branched saturated or unsaturated carbon chain of 1 to 8 C atoms, and

F² has, independently of F¹, the same meaning as F¹,

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G¹ is a bond or can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R⁵ radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, and

G² is NR⁴¹R⁴² and



or a bond, and

G³ can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical radicals R⁵, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is

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- hydrogen, and
- p can be 0 and 1 and
- s can be 0 and 1 and
- q can be 0 and 1 and
- r can be 0 and 1 and
- R⁴¹ can be hydrogen C₁-C₆-alkyl, it being possible for each carbon atom also to carry up to two R⁶ radicals, phenyl which may also carry a maximum of two R⁶ radicals, and (CH₂)_t-K and
- R⁴² can be hydrogen, C₁-C₆-alkyl, -CO-R⁸, CO₂-R⁸, SO₂NH₂, SO₂-R⁸, -(C=NH)-R⁸ and -(C=NH)-NHR⁸ and
- R⁴³ can be hydrogen and C₁-C₄-alkyl and
- t can be 1, 2, 3, 4 and
- K can be NR¹¹R¹², NR¹¹-C₁-C₄-alkyl-phenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, homopiperidine, piperazine, which may also be substituted by an alkyl radical C₁-C₆-alkyl, and homopiperazine which may also be substituted by an alkyl radical C₁-C₆-alkyl, and
- R⁵ can be hydrogen, chlorine, fluorine, bromine, iodine, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, C₁-C₄-alkyl-CO-NH-R¹³, COR⁸, C₀-C₄-alkyl-O-CO-R¹³, C₁-C₄-alkyl-phenyl, phenyl, CO₂-C₁-C₄-alkyl, and branched and unbranched C₁-C₆-alkyl, O-C₁-C₄-alkyl, S-C₁-C₄-alkyl, it being possible for each C atom of the alkyl

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chains to carry up to two R^6 radicals, and for the alkyl chains also to be unsaturated, and,

R^6 can be hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C_1 - C_6 -alkyl, OH, nitro, CF_3 , CN, $NR^{11}R^{12}$, $NH-CO-R^{13}$, $O-C_1$ - C_4 -alkyl,

R^7 can be hydrogen, C_1 - C_6 -alkyl, phenyl, it being possible for the ring also to be substituted by up to two R^{71} radicals, and an amine $N^{11}R^{12}$ or a cyclic saturated amine which has 3 to 7 members and may also be substituted by an alkyl radical C_1 - C_6 -alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1 - C_6 -alkyl, and homopiperazine which may also be substituted by an alkyl radical C_1 - C_6 -alkyl,

and where the radicals R^{11} , R^{12} and R^{13} in K, R^5 , R^6 and R^7 may, independently of one another, assume the same meaning as for R^1 , and

R^{71} can be OH, C_1 - C_6 -alkyl, $O-C_1$ - C_4 -alkyl, chlorine, bromine, iodine, fluorine, CF_3 , nitro, NH_2 , and

R^8 can be C_1 - C_6 -alkyl, CF_3 , phenyl, C_1 - C_4 -alkyl-phenyl, it being possible for the ring also to be substituted by up to two R^{81} radicals, and

R^{81} can be OH, C_1 - C_6 -alkyl, $O-C_1$ - C_4 -alkyl, chlorine, bromine, iodine, fluorine, CF_3 , nitro NH_2 , and

R^9 can be hydrogen, C_1 - C_6 -alkyl, C_1 - C_4 -alkyl-phenyl, CO_2 - C_1 - C_4 -alkyl-phenyl, CO_2 - C_1 - C_4 -alkyl, SO_2 -phenyl, COR^8 and phenyl, it being possible for the phenyl rings also to be substituted by up to two R^{91} radicals, and

its tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof.

2. A compound of the formula I as claimed in claim 1, where
A is a C₂ chain, which may be substituted, and
X¹ is O, and
R¹ is hydrogen.
3. A compound of the formula I as claimed in claim 1, in which
B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R⁵ radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.
4. A compound of the formula I as claimed in claim 3, where
B is phenyl, cyclohexyl, piperidine, pyridine, pyrimidine, pyrrole, pyrazole, thiophene, furan, oxazole, naphthalene, piperazine, quinoline, pyrazine,

5. A compound of the formula I as claimed in claim 4, where

D is O and NR^{43} , where R^{43} is hydrogen and C_1 - C_3 -alkyl and

6. A compound of the formula I as claimed in claim 1, in which B is L_v-Y-M_w , where

w is 1, and

M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R⁴ radicals and a maximum of two different or identical R⁵ radicals, and

R^4 is $D_{0,1}-F^1_{0,1}-G^1-G^2-G^3$, with G^3 equal to hydrogen, and

D is O and NR⁴³, where R⁴³ is hydrogen and C₁-C₃-alkyl and

7. A drug comprising one or more compounds of the formula I as claimed in claim 1 in addition to conventional carriers and excipients.

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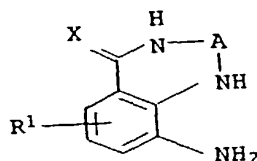
CLAIMS - OZ 50761

- C₁-C₆-alkyl chain, for producing drugs with a PARP-inhibiting effect.
9. The use of compounds of the formula I as claimed in claim 8 for producing drugs for treating neurodegenerative disorders and neuronal damage.
 10. The use as claimed in claim 8 for treating neurodegenerative disorders and neuronal damage caused by ischemia, trauma or massive bleeding.
 11. The use as claimed in claim 8 for treating stroke and craniocerebral trauma.
 12. The use as claimed in claim 8 for treating Alzheimer's disease, Parkinson's disease and Huntington's disease.
 13. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of prophylaxis of damage due to ischemias.
 14. The use of compound of the formula I as claimed in claim 8 for producing drugs for the treatment of epilepsies, in particular of generalized epileptic seizures, such as, for example, petit mal and tonoclonic seizures and partial epileptic seizures, such as temporal lobe, and complex partial seizures.
 15. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the kidneys after renal ischemia, damage caused by drug therapy such as, for example, during cyclosporin therapy, and for treatment during and after kidney transplants.
 16. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the heart following cardiac ischemia.
 17. The use of compounds of the formula I as claimed in claim 8 for producing drugs

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- for the treatment of microinfarcts such as, for example, during and after heart valve replacement, aneurysm resections and heart transplants.
18. The use of compounds of the formula I as claimed in claim 8 for producing drugs for treatment in cases of revascularization of critically narrowed coronary arteries such as, for example in PTCA and bypass operations or of critically narrowed peripheral arteries, especially leg arteries.
 19. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of acute myocardial infarct and of damage during and after medical or mechanical lysis thereof.
 20. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of tumors and metastasis thereof.
 21. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of sepsis, of multiorgan failure such as, for example, during septic shock and of acute respiratory distress syndrome.
 22. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of immunological disorders such as inflammations and rheumatic disorders such as, for example, rheumatoid arthritis.
 23. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of diabetes mellitus.
 24. A compound of the formula III

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III

in which

A is a C₁-C₃ chain it being possible for each carbon atom also to carry one or two of the following substituents: C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, CO₂H, Co₂-C₁-C₄-alkyl and phenyl or one C atom may also carry an =O group, and

X¹ and R¹ have the meanings stated in claim 1,

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,

6,8-diamino-2,4-(1H,3H)-quinazolinedione,

8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

25. A process for preparing compounds of the formula III and salts thereof, wherein 2-halo-3-nitrobenzoic esters are reacted with a suitable diamine in a polar solvent in the presence of a base, and then the nitro group is hydrogenated with hydrogen in the presence of a suitable catalyst.

26. The use of compounds of the formula III in the synthesis of PARP inhibitors.

Benzodiazepine derivatives, the preparation and use thereof

The present invention relates to novel benzodiazepine derivatives, their preparation and the use as inhibitors of the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30) for
5 producing drugs.

Poly(ADP-ribose) polymerase (PARP) or, as it is also called, poly(ADP-ribose) synthase (PARS) is a regulatory enzyme which is
10 found in cell nuclei (K. Ikai et al., J. Histochem. Cytochem. 1983, 31, 1261-1264). It is assumed that PARP is involved in the repair of DNA breaks (M.S. Satoh et al., Nature 1992, 356, 356-358). Damage or breaks in DNA strands activate the enzyme PARP which, when it is activated, catalyzes the transfer of
15 ADP-ribose from NAD (S. Shaw, Adv. Radiat. Biol., 1984, 11, 1-69). During this, nicotinamide is released from NAD. Nicotinamide is converted back into NAD by other enzymes with consumption of the energy carrier ATP. Overactivation of PARP would accordingly result in nonphysiologically large consumption
20 of ATP, and this leads in the extreme case to cell damage and cell death.

It is known that free radicals such as superoxide anion, NO and hydrogen peroxide may lead to DNA damage in cells and thus
25 activate PARP. The formation of large amounts of free radicals is observed in a number of pathophysiological states, and it is assumed that this accumulation of free radicals leads or contributes to the observed cell or organ damage. This includes, for example, ischemic states of organs as in stroke, myocardial infarct (C. Thiemermann et al., Proc. Natl. Acad. Sci. USA, 1997,
30 94, 679-683) or ischemia of the kidneys, but also reperfusion damage as occurs, for example, after lysis of myocardial infarct (see above: C. Thiemermann et al.). Inhibition of the enzyme PARP might accordingly be a means of at least partly preventing or
35 moderating this damage. PARP inhibitors might thus represent a novel therapeutic principle for treating a number of diseases.

The enzyme PARP influences the repair of DNA damage and might thus also play a part in the therapy of cancers, since a greater
40 action potential on tumor tissue was observed (G. Chen et al. Cancer Chemo. Pharmacol. 1988, 22, 303) in combination with substances with cytostatic activity.

Nonlimiting examples of tumors are leukemia, glioblastomas,
45 lymphomas, melanomas, and carcinomas of the breast and cervix.

It has additionally been found that PARP inhibitors may show an immunosuppressant effect (D. Weltin et al. *Int. J. Immunopharmacol.* 1995, 17, 265-271).

- 5 It has likewise been discovered that PARP is involved in immunological disorders or diseases in which the immune system plays an important part, such as, for example, rheumatoid arthritis and septic shock, and that PARP inhibitors may show a beneficial effect on the course of the disease (H. Kröger et al. *Inflammation* 1996, 20, 203-215; W. Ehrlich et al. *Rheumatol. Int.* 1995, 15, 171-172; C. Szabo et al., *Proc. Natl. Acad. Sci. USA* 1998, 95, 3867-3872; S. Cuzzocrea et al. *Eur. J. Pharmacol.* 1998, 342, 67-76).
- 10
- 15 PARP means for the purpose of this invention also isoenzymes of the PARP enzyme described above.

In addition, the PARP inhibitor 3-aminobenzamide showed protective effects in a model of circulatory failure (S.

- 20 Cuzzocrea et al., *Br. J. Pharmacol.* 1997, 121, 1065-1074). There is likewise experimental evidence that inhibitors of the enzyme PARP might be of benefit as agents for treating diabetes mellitus (V. Burkart et al. *Nature Med.* 1999, 5, 314-319).
- 25 Benzodiazepines and benzodiazepinones and their derivatives represent a class of chemicals which have been widely used in organic synthesis. Derivatives of these compounds additionally having a fused-on imidazo ring, that is to say imidazobenzodiazepinones, have scarcely been described, however.
- 30 Aminodibenzodiazepinones were prepared in P.V. Khadikar et al. *J. Heterocycl. Chem.* 1998, 35, 675. Thus, simple derivatives having radicals such as chlorine or nitro on the benzo ring and a methyl group on the imidazo ring were prepared in Geneste et al., *Eur. J. Chem. Chim. Ther.* 1978, 13, 53. In M.J. Kukla et al., *J. Med. Chem.* 1991, 34, 3187, a dihydroimidazobenzodiazepinone was prepared as intermediate for active substances said to have an anti-HIV effect.
- 35

- The compounds of the general formula I according to this
- 40 invention have not previously been described and are accordingly novel.

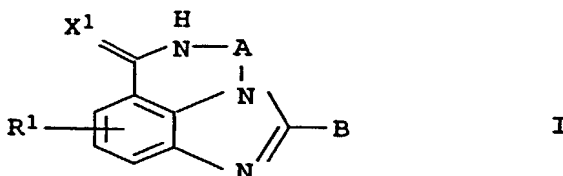
- It has additionally been found, surprisingly, that benzodiazepine derivatives having a fused-on ring are very effective inhibitors
- 45 of the enzyme PARP.

3

The present invention describes novel benzodiazepine derivatives of the general formula I which are potent PARP inhibitors.

The present invention relates to substituted benzodiazepine derivatives of the general formula I

10



I

in which

15 A can be a C₁-C₃ chain where each carbon atom may also carry one or two of the following substituents: C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, COOH, COO-C₁-C₄-alkyl and phenyl or one C atom may also carry an =O group, and

20 X¹ can be S, O and NH, and

R¹ is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C₁-C₆-alkyl, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, O-C₁-C₄-alkyl, where R¹¹ and R¹² are, independently
25 of one another, hydrogen or C₁-C₄-alkyl, and R¹³ is hydrogen, C₁-C₄-alkyl, C₁-C₄-alkyl-phenyl or phenyl, and

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated
30 mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by one R⁴ and a maximum of 3 different or identical R⁵ radicals, and
35 one or two carbon or sulfur atoms may also carry one or two =O groups, such as, for example, keto groups, sulfones or sulfoxides, or is a radical L_v-Y-M_w in which

L can be a straight-chain or branched, saturated or
40 unsaturated carbon chain of 1 to 8 C atoms, it being possible for each carbon atom to be substituted by one or two R⁴ radicals and a maximum of two different or identical R⁵ radicals, and

45 M has, independently of L, the same meaning as L, and

4

Y is a bond, or can be S, O or NR^3 , where R^3 can be hydrogen, branched and unbranched $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_1\text{-C}_4\text{-alkyl-phenyl}$, phenyl, and

5 v can be 0 and 1, and

w can be 0 and 1, and

when Y is a bond, R^4 and R^5 are not both hydrogen, and

10

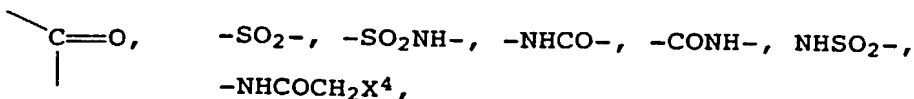
when B is $\text{L}_v\text{-Y-M}_w$, R^1 is not chlorine or NO_2 , and

R^4 is hydrogen and $-(\text{D})_p-(\text{E})_s-(\text{F}^1)_q-\text{G}^1-(\text{F}^2)_r-(\text{G}^2)-\text{G}^3$, where

15 D can be S, NR^{43} and O

E can be phenyl,

20



and

X^4 can be S, O or NH, and

25 F^1 can be a straight-chain or branched saturated or unsaturated carbon chain of 1 to 8 C atoms, and

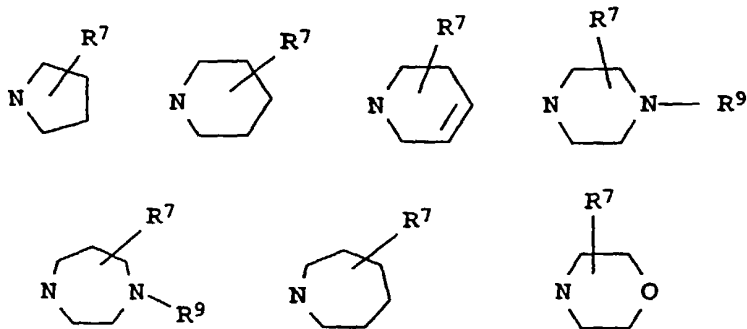
F^2 has, independently of F^1 , the same meaning as F^1 ,

30 G^1 is a bond or can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two $=\text{O}$ groups, and

40 G^2 is $\text{NR}^{41}\text{R}^{42}$ and

5

5



10

or a bond, and

15 G^3 can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical radicals R^5 , and 20 by a maximum of 3 different or identical radicals R^5 , and one or two carbon or sulfur atoms may also carry one or two =O groups, or is hydrogen, and

25 p can be 0 and 1 and

s can be 0 and 1 and

q can be 0 and 1 and

30 r can be 0 and 1 and

R^{41} can be hydrogen, C_1 - C_6 -alkyl, it being possible for each carbon atom also to carry up to two R^6 radicals, phenyl which may also carry a maximum of two R^6 radicals, and $(CH_2)_t$ -K and

35

R^{42} can be hydrogen, C_1 - C_6 -alkyl, $-CO-R^8$, CO_2-R^8 , SO_2NH_2 , SO_2-R^8 , $-(C=NH)-R^8$ and $-(C=NH)-NHR^8$ and

R^{43} can be hydrogen and C_1 - C_4 -alkyl and

40

t can be 1, 2, 3, 4 and

K can be $NR^{11}R^{12}$, NR^{11} - C_1 - C_4 -alkyl-phenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, 45 homopiperidine, piperazine, which may also be substituted by

6

an alkyl radical C₁-C₆-alkyl, and homopiperazine which may also be substituted by an alkyl radical C₁-C₆-alkyl, and

5 R⁵ can be hydrogen, chlorine, fluorine, bromine, iodine, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, C₁-C₄-alkyl-CO-NH-R¹³, COR⁸, C₀-C₄-alkyl-O-CO-R¹³, C₁-C₄-alkyl-phenyl, phenyl, CO₂-C₁-C₄-alkyl, and branched and unbranched C₁-C₆-alkyl, O-C₁-C₄-alkyl, S-C₁-C₄-alkyl, it being possible for each C atom of the alkyl chains to carry up to two R⁶ radicals, and for the alkyl chains also to be unsaturated, and

10 R⁶ can be hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C₁-C₆-alkyl, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, O-C₁-C₄-alkyl,

15 R⁷ can be hydrogen, C₁-C₆-alkyl, phenyl, it being possible for the ring also to be substituted by up to two R⁷¹ radicals, and an amine NR¹¹R¹² or a cyclic saturated amine which has 3 to 7 members, and may also be substituted by an alkyl radical C₁-C₆-alkyl, and homopiperazine which may also be substituted by an alkyl radical C₁-C₆-alkyl,

20 and where the radicals R¹¹, R¹² and R¹³ in K, R⁵, R⁶ and R⁷ may, independently of one another, assume the same meaning as for R¹, and

25 R⁷¹ can be OH, C₁-C₆-alkyl, O-C₁-C₄-alkyl, chlorine, bromine, iodine, fluorine, CF₃, nitro, NH₂, and

30 R⁸ can be C₁-C₆-alkyl, CF₃, phenyl, C₁-C₄-alkyl-phenyl, it being possible for the ring also to be substituted by up to two R⁸¹ radicals, and

35 R⁸¹ can be OH, C₁-C₆-alkyl, O-C₁-C₄-alkyl, chlorine, bromine, iodine, fluorine, CF₃, nitro, NH₂, and

40 R⁹ can be hydrogen, C₁-C₆-alkyl, C₁-C₄-alkyl-phenyl, CO₂-C₁-C₄-alkyl-phenyl, CO₂-C₁-C₄-alkyl, SO₂-phenyl, COR₈ and phenyl, it being possible for the phenyl rings also to be substituted by up to two R⁹¹ radicals, and

R⁹¹ can be OH, C₁-C₆-alkyl, O-C₁-C₄-alkyl, chlorine, bromine, iodine, fluorine, CF₃, nitro, NH₂,

45 and their tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof.

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7

Preferred compounds of the formula I are those where

A is a C₂ chain, which may be substituted, and

5 X¹ is O, and

R¹ is hydrogen.

Preferred compounds of the formula I are those as indicated
10 above, in which

B can be an unsaturated, saturated or partially unsaturated
mono-, bi- or tricyclic ring with a maximum of 15 carbon
atoms, an unsaturated, saturated or partially unsaturated
15 mono-, bi- or tricyclic ring with a maximum of 14 carbon
atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to
2 sulfur atoms, each of which may also be substituted by one
R⁴ and a maximum of 3 different or identical R⁵ radicals, and
one or two carbon or sulfur atoms may also carry one or two
20 =O groups.

Particularly preferred radicals for B are:

B phenyl, cyclohexyl, piperidine, pyridine, pyrimidine,
25 pyrrole, pyrazole, thiophene, furan, oxazole, naphthalene,
piperazine, quinoline, pyrazine, which may also be
substituted by one R⁴ or a maximum of 2 R⁵.

Very particularly preferred compounds of the formula I are those
30 where

R⁴ is hydrogen or D_{0,1}-F¹_{0,1}-G²-G³ with G³ equal to hydrogen and

D is O and NR⁴³, where R⁴³ is hydrogen and C₁-C₃-alkyl and
35

F¹ is C₂-C₄-alkyl.

Additional particularly preferred compounds of the formula I are
those where B is L_v-Y-M_w where

40

v is 0, and

w is 1, and

45 y is a bond, and

8

- M can be a straight-chain or branched carbon chain of 2 to 8 C atoms, which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R^4 radicals and a maximum of two different or identical R^5 radicals, and
- 5 R^1 is hydrogen, and
- R^4 is $D_{0,1}-F^1_{0,1}-G^1-G^2-G^3$ with G^3 equal to hydrogen, and
- 10 D is O and NR^{43} , where R^{43} is hydrogen and C_1-C_3 -alkyl and
- F^1 is C_2-C_4 -alkyl.
- 15 The use of compounds of the general formula I for producing medicines with a PARP-inhibiting effect is likewise claimed, with R^1 , X^1 and A having the same meaning as above, and it being possible for B to be hydrogen and a C_1-C_6 alkyl chain.
- 20 The compounds of the formula I can be employed as racemates, as enantiomerically pure compounds or as diastereomers. If enantiomerically pure compounds are required, they can be obtained, for example, by carrying out a conventional racemate resolution with the compounds of the formula I or their
- 25 intermediates using a suitable optically active base or acid.
- Alkyl chains may in each case be branched or unbranched. Unbranched alkyl chains are preferred.
- 30 The invention thus also relates to compounds which are mesomers or tautomers of compounds of the formula I.

The invention further relates to the physiologically tolerated salts of the compounds I, which can be obtained by reacting

35 compounds I with a suitable acid or base. Suitable acids and bases are listed, for example, in Fortschritte der Arzneimittelforschung, 1966, Birkhäuser Verlag, volume 10, pages 224-285. These include, for example, hydrochloric acid, citric acid, tartaric acid, lactic acid, phosphoric acid,

40 methanesulfonic acid, acetic acid, formic acid, maleic acid, fumaric acid etc., and sodium hydroxide, lithium hydroxide, potassium hydroxide and tris.

Prodrugs mean compounds which are metabolized in vivo to

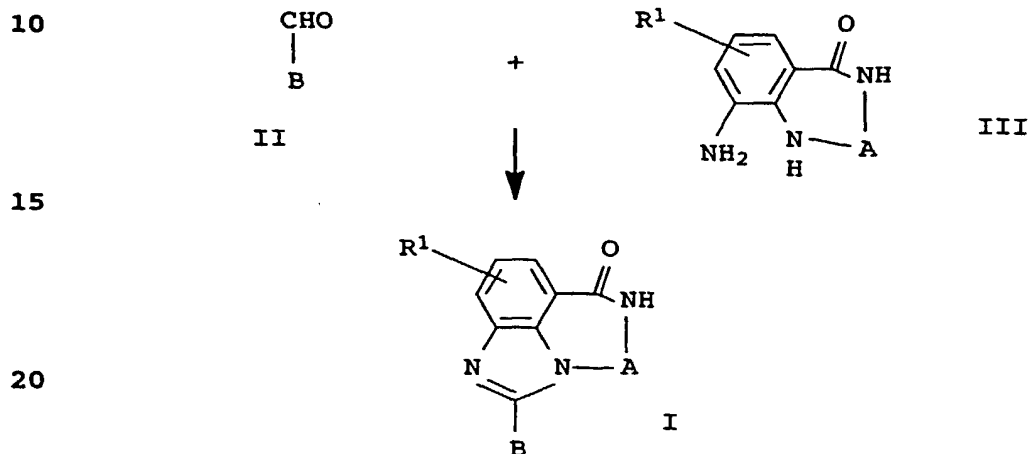
45 compounds of the general formula I. Typical prodrugs are phosphates, carbamates of amino acids, esters and others.

9

The benzodiazepine derivatives I according to the invention can be prepared in various ways, as outlined in synthesis schemes 1-3.

5 The possible methods of synthesis are essentially already known or are based on analogous routes which are known.

Synthesis scheme 1



Condensation of the aldehyde II with diamines III results in the
25 benzimidazole I, this preferably being done in polar solvents
such as ethanol or dimethylformamide with addition of acids such
as acetic acid at elevated temperature, ordinarily 80-120°C. It is
beneficial for the reaction to add weak oxidizing agents such as,
for example, copper(II) salts which are added, for example, as
30 aqueous solutions.

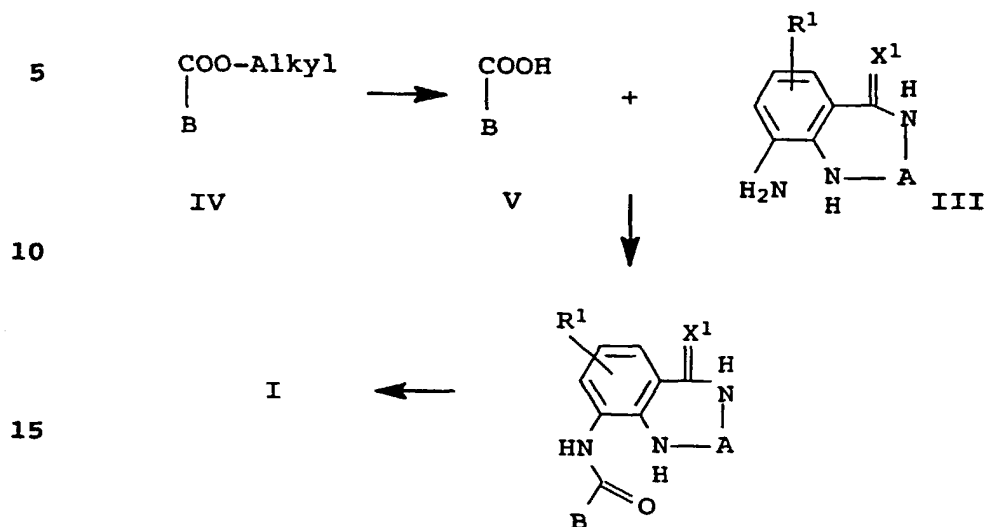
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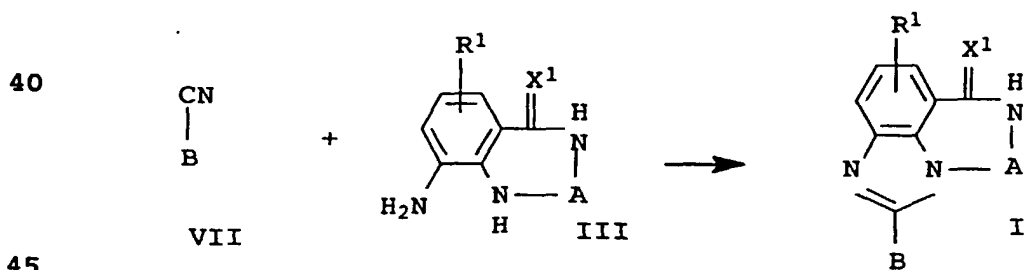
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Scheme 2



As an alternative to the aldehydes II shown in scheme I, it is also possible to employ acids such as V (see scheme 2) or nitriles such as VII (see scheme 3) in place of the aldehyde. Reaction of these derivatives takes place in analogy to the preparation from the substituted aldehydes II. Starting from V the condensation to II takes place in two stages. Firstly, the acid V is reacted with the aniline III in a peptide-like coupling to give the amide VI. This is carried out under conventional conditions which are listed, for example, in Houben-Weyl, Methoden der Organischen Chemie, 4th Edition, E5, chapter V, and R.C. Larock, Comprehensive Organic Transformations, VCH Publisher, 1989, pages 972 et seq. The ring closure to the benzimidazole then takes place at elevated temperature, for example 60 to 180°C, with or without solvents such as dimethylformamide, with the addition of acids such as acetic acid or directly in acetic acid itself.

Scheme 3



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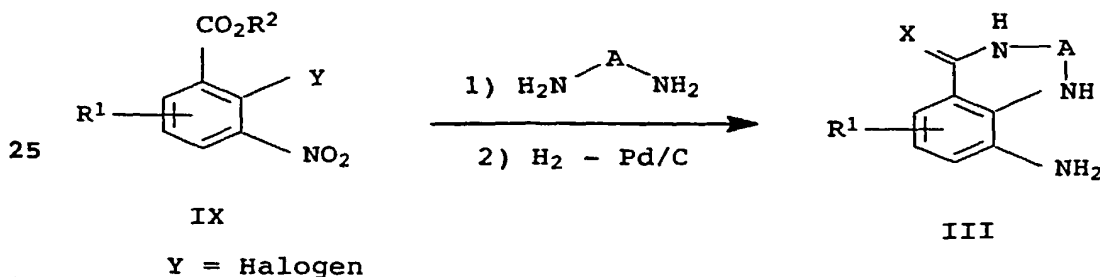
Reaction of the diamine III with a nitrile VII likewise takes place under conventional conditions. This may entail the use of solvents such as dimethylformamide with the addition of acids or else the use of polyphosphoric acid at elevated temperature such as 60 to 200°C. It is, however, also possible to use the conventional methods for preparing amidines from benzonitriles as described in Houben-Weyl, Methoden der organischen Chemie, E5, pages 1304 et seq., J. Amer. Chem. Soc. 1957, 427 and J. Org. Chem. 1987, 1017.

10

Compounds III are synthesized as shown in scheme 4 by reacting a substituted nitrobenzoic ester IX with a suitable diamine in a polar solvent such as dimethylformamide in the presence of a base such as potassium carbonate at 100°C to 150°C, preferably at 110°C to 130°C, in particular at about 120°C, followed by hydrogenation in the presence of a suitable catalyst such as 10% palladium on carbon.

Scheme 4

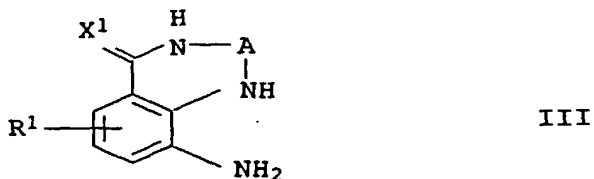
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30

The invention additionally relates to the intermediates of the formula III

35



40 in which

A is a C₁-C₃ chain it being possible for each carbon atom also to carry one or two of the following substituents: C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, CO₂H, CO₂-C₁-C₄-alkyl and phenyl or one C atom may also carry an =O group, and

45

12

X¹ and R¹ have the meanings stated previously,

excluding the compounds

- 9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,
5 9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,
6,8-diamino-2,4-(1H,3H)-quinazolinedione,
8-amino-2,4-(1H,3H)-quinazolinedione
and the salts thereof.

- 10 Additionally a process for preparing compounds of the formula III and their salts, where 2-halo-3-nitrobenzoic esters are reacted with a suitable diamine in a polar solvent in the presence of a base, and then the nitro group is hydrogenated with hydrogen in the presence of a suitable catalyst,

15

and the use of compounds of the formula III in the synthesis of PARP inhibitors.

- The substituted benzodiazepine derivatives I contained in the
20 present invention are inhibitors of the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30).

- The inhibitory effect of the substituted benzodiazepine derivatives I can be determined using an enzyme assay which has
25 already been disclosed in the literature, with a K_i being determined as a gauge of the effect. The benzodiazepine derivatives I were measured in this way for an inhibitory effect on the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30).

- 30 The substituted benzodiazepine derivatives of the general formula I are inhibitors of poly(ADP-ribose) polymerase (PARP) or, as it is also called, poly(ADP-ribose) synthase (PARS) and can thus be used for the treatment and prophylaxis of diseases associated with an increased activity of these enzymes.

35

The compounds of the formula I can be employed to produce drugs for treating damage following ischemias and for the prophylaxis of expected ischemias in various organs.

- 40 The present benzodiazepine derivatives of the general formula I can accordingly be used for the treatment and prophylaxis of neurodegenerative disorders occurring after ischemia, trauma (craniocerebral trauma), massive bleeding, subarachnoid hemorrhages and stroke, and of neurodegenerative disorders such as
45 multi-infarct dementia, Alzheimer's disease, Huntington's disease and of epilepsies, in particular of generalized epileptic seizures such as, for example, petit mal and tonoclonic seizures

The pharmaceutical preparations according to the invention contain a therapeutically effective amount of the compounds I in addition to conventional pharmaceutical excipients.

30 For local external use, for example, in dusting powders, ointments or sprays, the active substances can be present in the usual concentrations. The active substances are ordinarily present in an amount of 0.001 to 1% by weight, preferably 0.001 to 0.1% by weight.

For internal use, the preparations are administered in single doses. From 0.1 to 100 mg are given per kg of body weight in a single dose. The preparation may be administered in one or more doses each day, depending on the nature and severity of the disorders.

Appropriate for the required mode of administration, the pharmaceutical preparations according to the invention comprise conventional carriers and diluents, in addition to the active
45 substance. For local external use, it is possible to use pharmaceutical excipients such as ethanol, isopropanol, ethoxylated castor oil, ethoxylated hydrogenated castor oil,

14

polyacrylic acid, polyethylene glycol, polyethylene glycol stearate, ethoxylated fatty alcohols, liquid paraffin, petrolatum and wool fat. Examples suitable for internal use are lactose, propylene glycol, ethanol, starch, talc and polyvinylpyrrolidone.

5

It is also possible for antioxidants such as tocopherol and butylated hydroxyanisole, and butylated hydroxytoluene, flavor-improving additives, stabilizers, emulsifiers and lubricants to be present.

10

The substances present in the preparation in addition to the active substance, and the substances used in the production of the pharmaceutical preparations are toxicologically acceptable and compatible with the particular active substance. The

15 pharmaceutical preparations are produced in a conventional way, for example by mixing the active substance with conventional carriers and diluents.

The pharmaceutical preparations can be administered in various

20 ways, for example orally, parenterally such as intravenously by infusion, subcutaneously, intraperitoneally and topically. Thus, possible presentations are tablets, emulsions, infusion and injection solutions, pastes, ointments, gels, cremes, lotions, dusting powders and sprays.

25

Pharmacological example:

Inhibition of the enzyme poly(ADP-ribose) polymerase or PARP (EC 2.4.2.30)

30 A 96-well microtiter plate (Falcon) is coated with histones (type II-AS; SIGMA H7755). For this purpose, histones are dissolved in a concentration of 50 µg/ml in carbonate buffer (0.05 M NaHCO₃; pH 9.4). The individual wells of the microtiter plates are each incubated with 100 µl of this histone solution overnight. The

35 histone solution is then removed, and the individual wells are incubated with 200 µl of a 1% strength BSA (bovine serum albumin) solution in carbonate buffer at room temperature for 2 hours. This is followed by washing three times with washing buffer (0.05% Tween10 in PBS). For the enzyme reaction, 50 µl of the

40 enzyme reaction solution (5 µl of reaction buffer (1 M tris-HCl pH 8.0, 100 mM MgCl₂, 10 mM DTT), 0.5 µl of PARP (c = 0.22 µg/µl), 4 µl of activated DNA (SIGMA D-4522, 1 mg/ml in water), 40.5 µl of H₂O) are preincubated in each well with 10 µl of an inhibitor solution for 10 minutes. The enzyme reaction is started by adding

45 40 µl of a substrate solution (4 µl of reaction buffer (see above), 8 µl of NAD solution (100 µM in H₂O), 28 µl of H₂O). The reaction time is 20 minutes at room temperature. The reaction is

Examples

30

a) 9-Nitro-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one
35 24 g (0.11 mol) of methyl 2-chloro-3-nitrobenzoate were dissolved in 250 ml of dimethylformamide. 15.4 g (0.11 mol) of potassium carbonate and 22.3 ml (0.33 mol) of ethylenediamine were successively added, and the mixture was heated at 120°C for 3 hours. The mixture was then
40 concentrated to half the volume in vacuo, and the residue was poured into water, whereupon the product precipitated. 19.7 g of the product were obtained.

b) 9-Amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one
45 1.7 g of 10% palladium/carbon were added to 19 g (91.7 mmol)
of the intermediate 1a in 500 ml of ethanol, and it was then
hydrogenated with hydrogen. The mixture was then filtered.

16

The filtrate was concentrated in vacuo, and the residue was recrystallized from isopropanol/ether. The crystals which separated out were filtered off with suction. 14.4 g of the product were obtained.

- 5
- c) 2-(4-(4-Methylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 2.0 g (11.3 mmol) of the intermediate 1b and 2.8 ml (45.15 mmol) of concentrated acetic acid were dissolved in
- 10 200 ml of methanol and, at room temperature, a solution of 3.0 g (14.7 mmol) of 4-(4-methylpiperazin-1-yl)benzaldehyde in 50 ml of methanol was added dropwise. The mixture was stirred at room temperature for 1 hour. Then 2.9 g (14.7 mmol) of copper(II) acetate dissolved in 100 ml of
- 15 water were added dropwise, and the mixture was refluxed for 30 minutes. During this time, in parallel a solution of 4.1 g (17 mmol) of sodium sulfide x 9 H₂O in 70 ml of water and a solution of 17 ml of 1 M hydrochloric acid in 50 ml of water were added. After cooling, the resulting precipitate was
- 20 filtered off with suction, and the filtrate was concentrated in vacuo. The resulting residue was partitioned between aqueous sodium bicarbonate solution and ethyl acetate. The organic phase was separated off, dried and concentrated in vacuo. The residue was crystallized from ethyl acetate/ether.
- 25 2.4 g of the product were obtained.

¹H-NMR (D₆-DMSO): δ = 2.2 (3H), 2.5 (4H), 3.3 (4H), 3.5 (2H), 4.4 (2H), 7.1 (2H), 7.3 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm. [M⁺ = 361]

30

Example 2

2-(4-Nitrophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

35

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-nitrobenzaldehyde.

- 40 ¹H-NMR (D₆-DMSO): δ = 3.6 (2H), 4.5 (2H), 7.4 (1H) and 7.9-8.6 (7H) ppm. [M⁺ = 308]

45

17

Example 3

2-(4-(2-N,N-Diethylaminoeth-1-yloxy)phenyl)-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

5

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(2-N,N-diethylaminoeth-1-yloxy)benzaldehyde.

10 ¹H-NMR (D₆-DMSO): δ = 1.0 (6H), 2.6 (4H), 2.8 (1H), 3.5 (2H), 4.1 (2H), 4.5 (2H), 7.1 (2H), 7.4 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.
[M⁺ = 378]

15 The following further examples were prepared in analogy to the above methods:

Example 4

20 2-(4-(2-Piperidin-1-yleth-1-yloxy)phenyl)-5,6-dihydroimidazo-[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and

25 4-(2-piperidin-1-yleth-1-yloxy)benzaldehyde.

¹H-NMR (D₆-DMSO): δ = 1.3-1.6 (6H), 2.5 (4H), 2.7 (2H), 3.6 (2H), 4.2 (2H), 4.5 (2H), 7.1 (2H), 7.4 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.

30 [M⁺ = 390]

Example 5

2-(4-(N-(2-N,N-Diethylaminoeth-1-yl)-N-methylamino)phenyl)-5,6-
35 dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4(N-(2-N,N-diethylaminoeth-1-yl)-N-methylamino)benzaldehyde.

40

¹H-NMR (D₆-DMSO): δ = 0.9 (6H), 2.5 (6H), 3.0 (3H), 3.4-3.6 (4H), 4.45 (2H), 6.8 (2H), 7.3 (1H), 7.6-7.9 (4H) and 8.45 (1H) ppm.
[M⁺ = 391]

45

18

Example 6

2-(4-(4-(tert-Butyloxycarbonyl)piperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

5

The product was obtained in analogy to the method in 1c from 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(4-(tert-butyloxycarbonyl)piperazin-1-yl)benzaldehyde.

- 10 ¹H-NMR (D₆-DMSO): δ = 1.4 (9H), 3.3 (4H), 3.4-3.6 (6H), 4.45 (2H), 7.1 (2H), 7.3 (1H), 7.7-7.9 (4H) and 8.4 (1H) ppm.
[M⁺ = 447]

Example 7

15

2-(4-(4-(tert-Butyloxycarbonyl)homopiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was obtained in analogy to the method in 1c from

- 20 9-amino-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one and 4-(4-(tert-butyloxycarbonyl)homopiperazin-1-yl)benzaldehyde.

¹H-NMR (D₆-DMSO): δ = 1.2-1.3 (9H), 1.8-1.9 (2H), 3.2-3.8 (10H), 4.45 (2H), 6.9 (2H), 7.3 (1H), 7.7 (2H), 7.8 (2H) and

- 25 8.4 (1H) ppm.
[M⁺ = 461]

Example 8

- 30 2-(4-(Homopiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

The product was prepared from the product from Example 7 in analogy to Example 9.

- 35 [M⁺ = 361]

Example 9

- 2-(4-(Piperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-
40 [1,4]benzodiazepin-7(4H)-one trihydrochloride

0.5 g of Example 6 was added to 30 ml of isopropanolic hydrogen chloride solution at room temperature and stirred for several hours. The mixture was then concentrated in vacuo, and the

- 45 resulting residue was recrystallized from ethanol. The product was obtained as trihydrochloride.

19

¹H-NMR (D₆-DMSO): δ = 3.2-3.8 (10H), 4.5 (2H), 7.2 (2H), 7.5-8.0 (5H), 8.6 (1H) and 9.6 (broad) ppm.
[M⁺ = 347]

5 Example 10

2-(4-Aminophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times 2 HCl
[M⁺ = 280]

10 Example 11

2-(Piperidin-4-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl
[M⁺ = 271]

15 Example 12

2-(1-n-Propylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl
[M⁺ = 313]

20 Example 13

2-(1-Benzylpiperidin-4-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl
[M⁺ = 361]

25 Example 14

2-(Pyridin-4-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl
[M⁺ = 265]

30 Example 15

2-(Thien-3-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl
[M⁺ = 270]

35 Example 16

2-(Quinolin-3-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl
[M⁺ = 315]

40 Example 17

2-(Naphth-2-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺ = 313]

45 Example 18

2-(1H-Imidazol-1-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one \times HCl

[M⁺ = 330]

Example 19

2-(4-(3-Formylpyrrol-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-
5 [1,4]benzodiazepin-7(4H)-one
[M⁺ = 356]

Example 20

2-(4-(3-Trifluoroacetamidomethylpyrrol-1-yl)phenyl)-5,6-di-
10 hydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one x HCl
[M⁺ = 453]

Example 21

2-(4-(4-(Piperidin-1-yl)piperidin-1-yl)phenyl)-5,6-dihydro-
15 imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one x 2 HCl
[M⁺ = 432]

Example 22

2-(4-(3-(Piperidin-1-ylmethyl)pyrrol-1-yl)phenyl)-5,6-dihydro-
20 imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one x HCl
[M⁺ = 427]

Example 23

2-(4-(3-Aminomethylpyrrol-1-yl)phenyl)-5,6-dihydroimidazo-
25 [4,5,1-jk][1,4]benzodiazepin-7(4H)-one x HCl
[M⁺ = 358]

Example 24

2-(3-(2-(N,N-Dimethylamino)eth-1-yl)-4-nitrophenyl)-5,6-di-
30 hydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one x HCl
[M⁺ = 380]

Example 25

5,6-Dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
35 [M⁺ = 187]

Example 26

2-(Pyrazin-2-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-
7(4H)-one x HCl
40 [M⁺ = 266]

Example 27

2-(2-(tert-Butyloxycarbonylaminomethyl)thiazol-4-yl)-5,6-di-
hydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
45 [M⁺ = 399]

Example 28

2-(2-(Aminomethyl)thiazol-4-yl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one x HCl
[M⁺ = 300]

5

Example 29

2-(2-fluoro-4-(pyridin-4-yl)phenyl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺ = 358]

10

Example 30

2-(1-(1-Methylpiperidin-4-yl)piperidin-4-yl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one x 2 HCl
[M⁺ = 369]

15

Example 31

2-[(Z)-1-(4-Fluorophenyl)-2-(pyridin-3-yl)ethenyl]-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺ = 384]

20

Example 32

2-(1-Benzylpiperidin-3-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺ = 360]

25

Example 33

2-(1-Phenylcyclopent-1-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4*H*)-one
[M⁺ = 331]

30

Example 34

2-(1-Phenylcyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺ = 345]

35

Example 35

6-(4-(Aminomethyl)cyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺ = 298]

40

Example 36

2-[(E)-2-(Pyridin-4-yl)ethenyl]-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one
[M⁺ = 290]

45

Example 37

2-[3-Cyanophenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 288]

5

Example 38

2-(2-Phenyl-1*H*-imidazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]-benzodiazepin-7(4*H*)-one

$[M^+ - 1 = 329]$

10

Example 39

2-[2-(4-Methylphenyl)-1,3-oxazol-4-yl]-5,6-dihydroimidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 344]

15

Example 40

2-[1-(4-Fluorophenyl)-5-methyl-1*H*-pyrazol-4-yl]-5,6-dihydro-imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

[M⁺-1 = 361]

20

Example 41

2-[1-(4-Chlorophenyl)-1*H*-pyrazol-5-yl]-5,6-dihydroimidazo-
[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

[M⁺-1 = 363]

25

Example 42

2-(3-Propyl-5-isoxazolyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one

$[M^+ - 1 = 296]$

30

Example 43

2-[1-(4-Methoxyphenyl)-1*H*-pyrrol-3-yl]-5,6-dihydroimidazo-[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

$[M^+ - 1 = 358]$

35

Example 44

2-(1,2,5-Trimethyl-1*H*-pyrrol-3-yl)-5,6-dihydroimidazo-
[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

$[M^+ - 1 = 294]$

40

Example 45

2-(4-Benzoyl-1-methyl-1*H*-pyrrol-2-yl)-5,6-dihydroimidazo-
[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one

$$[M^+ - 1 = 370]$$

45

Example 46

2-{4-Methyl-5-[4-(trifluoromethyl)phenyl]-3-isoxazolyl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 412]

5

Example 47

2-(5-Methyl-2-furyl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 267]

10

Example 48

2-[1-(2-Chlorophenyl)-5-(trifluoromethyl)-1*H*-pyrazol-4-yl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 431]

15

Example 49

2-(5-Methyl-1*H*-imidazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 267]

20

Example 50

2-(1-Methyl-1*H*-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 267]

25

Example 51

2-(1-Methyl-1*H*-indol-3-yl)-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 316]

30

Example 52

2-{6-[(4-Chlorophenyl)thio]imidazo[2,1-*b*][1,3]thiazol-5-yl}-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 451]

35

Example 53

2-[1-(4-Chlorophenyl)-1*H*-pyrrol-3-yl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 363]

40

Example 54

2-[2-(4-Fluorobenzoyl)-1-benzofuran-5-yl]-5,6-dihydroimidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 425]

45

$[M^+ - 1 = 427]$

5

$$[M^+ - 1] = 3301$$

10

$$[M^+ - 1] = 278$$

15

$$[M^+ - 1] = 373$$

20

$$[M^+ - 1] = 399$$

25

$[M^+ - 1 = 329]$

30

 $[M^+ - 1] = 384$

35

$$\{M^+ - 1 = 4561$$

40

$$[M^+ - 1] = 3321$$

45

25

Example 64

2-[4-Bromo-1-(4-chlorobenzyl)-1H-pyrazol-5-yl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 456]

5

Example 65

2-[1-(4-Methylphenyl)-1H-pyrrol-2-yl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 342]

10

Example 66

2-(5-Chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 377]

15

Example 67

2-[4-(4-Chlorobenzoyl)-1-methyl-1H-pyrrol-2-yl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 404]

20

Example 68

2-[4-(Diethylamino)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 334]

25

Example 69

2-(4-Methoxy-1-naphthyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 343]

30

Example 70

2-(4-Methoxy-2,5-dimethylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 321]

35

Example 71

2-[3-(4-Chlorophenoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 389]

40

Example 72

2-[4-(Methylthio)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 309]

45

Example 73

2-[4-(Acetyloxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 321]

5

Example 74

2-[2,5-Bis(trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 399]

10

Example 75

2-(2,3-Dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 323]

15

Example 76

2-(2-Methylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 277]

20

Example 77

2-[4-(Benzyloxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 369]

25

Example 78

2-(2-Chloro-6-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 315]

30

Example 79

2-(2-Ethoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 307]

35

Example 80

2-(4-Isopropylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 305]

40

Example 81

2-(6-Nitro-1,3-benzodioxol-5-yl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 352]

45

Example 82

2-(2,3-Dihydro-1,4-benzodioxin-6-yl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 321]

5

Example 83

2-[4-(Dimethylamino)-1-naphthyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 355]

10

Example 84

2-[4-(Difluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 329]

15

Example 85

2-(3,7-Dichloro-8-quinolinyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 383]

20

Example 86

2-[4-Chloro-3-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 365]

25

Example 87

2-(1-tert-Butyl-1H-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 309]

30

Example 88

2-(4-Chloro-5-nitro-1-benzothien-2-yl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 398]

35

Example 89

2-[1-(4-Phthalimidobutan-1-yl)indol-3-yl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 503]

40

Example 90

2-(3-Isobutyl-5-isoxazolyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 310]

45

Example 91

2-[1-(4-Methoxyphenyl)-5-(trifluoromethyl)-1H-pyrazol-4-yl]-
5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 427]

5

Example 92

2-[2-(Dimethylamino)-1,3-thiazol-5-yl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 313]

10

Example 93

2-[3-(4-tert-Butylphenyl)-5-isoxazolyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 386]

15

Example 94

2-[1-(4-Chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]-5,6-dihydro-
imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 391]

20

Example 95

2-(3-Chlorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 297]

25

Example 9.6

2-(3-Fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin
-7(4H)-one
[M⁺-1 = 281]

30

Example 97

2-(3-Phthalimidophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 408]

35

Example 98

2-{4-[3-Chloro-5-(trifluoromethyl)-2-pyridinyl]phenyl}-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 442]

40

Example 99

2-[5-(6-Methylnicotinamido)-2-chlorophenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M⁺-1 = 431]

45

2-(4-tert-Butoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 335]

5

4-(7-Oxo-4,5,6,7-tetrahydroimidazo[4,5,1-jk][1,4]benzodiazepin-2-yl)benzonitrile
[M⁺-1 = 288]

10

2-[3-(Trifluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M⁺-1 = 347]

15

2-[3-(3,5-Dichlorophenoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 423]

20

2-(3-Bromo-4,5-dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 402]

25

2-[5-(Allyloxy)-1,3-dimethyl-1*H*-pyrazol-4-yl]-5,6-dihydroimidazo-
[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 337]

30

2-{2-[3-(Trifluoromethyl)anilino]phenyl}-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 422]

35

2-[2-(2-Phenylethyl)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 367]

40

2-(3-Benzoylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 367]

45

Example 109

2-(4-Acetamidophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 320]

5

Example 110

2-(1,3-Benzodioxol-5-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 307]

10

Example 111

2-(5-Aminosulfonyl-2,4-dichlorophenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 411]

15

Example 112

2-(2-Benzoyloxymethylphenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 397]

20

Example 113

2-(2-N,N-Diethylaminocarbonyl-3,6-difluor-phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 398]

25

Example 114

2-(2-(N-2,2,2-Trifluoracetamido)phenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 374]

30

Example 115

2-[4-(Trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 331]

35

Example 116

2-[2-Fluoro-4-(trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 349]

40

Example 117

2-(3-Chloro-4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 327]

45

Example 118

2-(3-Bromo-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 360]

5

Example 119

2-(2,5-Dimethyl-1-phenyl-1H-pyrrol-3-yl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 356]

10

Example 120

2-[4-(2,4-Dichlorobenzoyl)-1-methyl-1H-pyrrol-2-yl]-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 439]

15

Example 121

2-[1-(2-Fluorophenyl)-1H-pyrrol-2-yl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 346]

20

Example 122

2-(3,5-Dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 323]

25

Example 123

2-(4-Bromo-2-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 360]

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Example 124

2-(2-Chloro-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 315]

35

Example 125

2-[2-(Benzyloxy)-3-methoxyphenyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 399]

40

Example 126

2-(2,4-Diethoxy-3-methylphenyl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 365]

45

Example 127

2-(5-Bromo-2,4-dimethoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 402]

5

Example 128

2-[4-(Dimethylamino)-2-methoxyphenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 336]

10

Example 129

2-[2-Chloro-5-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 366]

15

Example 130

2-(3,5-Dimethylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 291]

20

Example 131

2-[4-Fluoro-2-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 349]

25

Example 132

2-(5-Bromo-2-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 360]

30

Example 133

2-[4-(1-Pyrrolidiny)phenyl]-5,6-dihydroimidazo[4,5,1-*jk*]-
[1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 332]

35

Example 134

2-(4-Isopropoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 321]

40

Example 135

2-(3,5-Dibromophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 421]

45

Example 136

2-[4-(Benzyloxy)-2-methoxyphenyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 399]

5

Example 137

2-[3-Fluoro-4-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 349]

10

Example 138

2-[5-(4-Nitrophenyl)-2-furyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 374]

15

Example 139

2-(3-Acetyloxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 321]

20

Example 140

2-[2-(tert-Butylthio)phenyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 351]

25

Example 141

2-[2-Fluoro-5-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 349]

30

Example 142

2-(3,4-Dimethylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 291]

35

Example 143

2-[4-(Ethylthio)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 323]

40

Example 144

2-{4-[(Trifluoromethyl)thio]phenyl}-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 363]

45

Example 154

2-(2,5-Dimethoxytetrahydro-3-furanyl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 317]

5

Example 155

2-(2-Thienyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-
7(4H)-one
[M⁺-1 = 269]

10

Example 156

2-(1,3-Thiazol-2-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 270]

15

Example 157

2-(4-Methoxycyclohexyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 299]

20

Example 158

2-(3,5-Dimethoxy-2-methoxycarbonylphenyl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7-(4H)-one
[M⁺-1 = 381]

25

Example 159

2-{5-[1-Methyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]-2-thienyl}-
5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 417]

30

Example 160

2-(2-Fluoro-5-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 311]

35

Example 161

2-(4-Butylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-
7(4H)-one
[M⁺-1 = 319]

40

Example 162

2-[2-(Trifluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 347]

45

Example 163

2-(4-Quinoliny)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 314]

5

Example 164

2-(2-Quinoliny)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 314]

10

Example 165

2-(2-Chloro-3-quinoliny)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 348]

15

Example 166

2-[4-(1H-Pyrrol-1-yl)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one

[M⁺-1 = 328]

20

Example 167

2-(1H-Indol-6-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 302]

25

Example 168

2-[4-(1,1-Dioxo-1,2-thiazinan-2-yl)-phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 396]

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Example 169

2-(1,3-Benzothiazol-6-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 320]

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Example 170

2-(2,3-Dihydro-1-benzofuran-5-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 305]

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Example 171

2-(4-(2-(2-Furylmethylthio)acetamido)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 432]

45

2-{[5-(2-Fluorobenzoyl)-2-thienyl]methyl}-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 405]

5

2-(2-(2-Acetamidopyridin-5-ylthio)pyridin-5-yl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 430]

10

2-(4-(N-(3,4-Dioxo-2-ethoxy-1-cyclobuten-1-yl)amino)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M⁺-1 = 402]

15

2-[(2-Quinoxalinylythio)methyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 361]

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2-[4-(Methylamino)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 292]

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2-(5-(4-Aminosulfonylphenyl)furan-2-yl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 408]

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2-{2,5-Dimethyl-1-[4-(trifluoromethyl)phenyl]-1*H*-pyrrol-3-yl}-
5,6-dihydroimidazo[4,5-*l*-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 424]

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2-{1-[(2,4-Difluorophenyl)sulfonyl]-1*H*-pyrrol-2-yl}-5,6-dihydro-
imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 428]

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2-{1-[2,6-Dichloro-4-(trifluoromethyl)phenyl]-2,5-dimethyl-1H-pyrrol-3-yl}-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

45 [M⁺-1 = 493]

2-[5-(Phenylethynyl)-2-thienyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 369]

5

2-{5-[2-(Trifluoromethoxy)phenyl]-2-furyl}-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 413]

10

2-(5-(2-Methoxycarbonylthiophen-3-yl)furan-2-yl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 393]

15

2-(2,5-Dimethylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 291]

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2-(4-Methoxycarbonylphenyl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 321]

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2-(4-Methylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 277]

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2-(3,4-Difluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 299]

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2-(4-Fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 281]

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2-(3-Chloro-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M⁺-1 = 315]

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Example 190

2-(3-Bromo-4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one

[M⁺-1 = 372]

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Example 191

2-[4-(Trifluoromethoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one

[M⁺-1 = 374]

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Example 192

2-(2,5-Difluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one

[M⁺-1 = 299]

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Example 193

2-[4-(1,1,2,2-Tetrafluoroethoxy)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 379]

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Example 194

2-[4-Fluoro-3-(trifluoromethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 349]

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Example 195

2-(4-Cyanophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one

[M⁺-1 = 288]

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Example 196

2-(3-Bromo-4-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one

[M⁺-1 = 360]

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Example 197

2-(4-tert-Butyl-2-methylphenyl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 333]

40

Example 198

2-[4-(1-Methoxy-1-methylethyl)phenyl]-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 335]

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2-(4-Bromophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-
7(4H)-one
[M⁺-1 = 342]

5

2-[4-(3,4-Dichlorophenoxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 424]

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2-[4-(2-Propynyloxy)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]-benzodiazepin-7(4H)-one
[M⁺-1 = 317]

15

2-{4-[Chloro(difluoro)methyl]phenyl}-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 347]

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2-(4-Benzoylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 367]

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2-(4-Ethylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-
7(4*H*)-one
[M⁺-1 = 291]

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2-(2-Hydroxy-5-methylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]-
benzodiazepin-7(4H)-one
[M⁺-1 = 293]

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2-[4-(2,6-Difluorobenzoyl)-1-methyl-1*H*-pyrrol-2-yl]-5,6-dihydro-
imidazo[4,5,1-*jk*][1,4]benzodiazepin-7(4*H*)-one
[M⁺-1 = 406]

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2-[4-(3-Chlorobenzoyl)-1-methyl-1H-pyrrol-2-yl]-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 404]

45

Example 208

2-(2-Ethoxy-1-naphthyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 357]

5

Example 209

2-[2-(Benzyloxy)-4,5-dimethoxyphenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 429]

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Example 210

2-{4-[(2-Chloroethyl)(ethyl)amino]-2-methylphenyl}-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 382]

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Example 211

2-(4,5-Dimethoxy-2-methylphenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 337]

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Example 212

2-(7-Methyl-2-naphthyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 327]

25

Example 213

2-(2,4-Dimethoxy-5-methylphenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 337]

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Example 214

2-(3-Benzoyl-2,4-dichlorophenyl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 436]

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Example 215

2-(6-Chloro-1,3-benzodioxol-5-yl)-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 341]

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Example 216

2-[4-(Benzyloxy)-3,5-dimethoxyphenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

[M⁺-1 = 429]

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Example 217

2-(3,4-Diethoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 351]

5

Example 218

2-(2-((Pyridin-2-yl)aminocarbonyl)eth-1-yl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 335]

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Example 219

2-(3-((Pyridin-2-yl)aminocarbonyl)prop-1-yl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 349]

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Example 220

2-((1,3-Dimethyl-3,7-dihydro-2,6-dioxo-1H-purin-8-yl)methyl-5,6-dihydroimidazo[4,5,1-jk]-[1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 379]

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Example 221

2-(2-((Thiazol-2-yl)aminocarbonyl)eth-1-yl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-2-yl)-7(4H)-one
[M⁺-1 = 341]

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Example 222

2-{2-[(1,3-Dimethyl-1H-pyrazol-5-yl)amino]phenyl}-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 372]

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Example 223

2-(2-(4-Chlorophenyl)methylthio-3-cyanopyridin-6-yl)-5,6-dihydro-
imidazo-[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 445]

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Example 224

2-(4-tert-Butylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
[M⁺-1 = 319]

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Example 225

2-{2,5-Dimethyl-1-[3-(trifluoromethyl)phenyl]-1H-pyrrol-3-yl}-
5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 424]

45

Example 226

2-(5-Chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 377]

5

Example 227

2-[2,5-Bis(trifluoromethyl)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 399]

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Example 228

2-[4-(4-tert-Butyl-1,3-thiazol-2-yl)phenyl]-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 402]

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Example 229

2-(3-Cyano-4-N,N-dimethylamino-2-fluorophenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 349]

20

Example 230

2-(6-Methoxy-2-naphthyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 343]

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Example 231

2-(4-Isobutylphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 319]

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Example 232

2-(3-Bromo-4-methoxyphenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
[M⁺-1 = 372]

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The following compounds according to the invention can be prepared in analogy to the methods described above:

1. 2-(4-(4-n-propylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
2. 2-(4-(4-isopropylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
3. 2-(4-(4-benzylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

44

4. 2-(4-(4-n-butylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
5. 2-(4-(4-ethylpiperazin-1-yl)phenyl)-5,6-dihydroimidazo-
5 [4,5,1-jk][1,4]benzodiazepin-7(4H)-one
6. 2-(4-(2-N,N-dimethylaminoeth-1-yloxy)phenyl)-5,6-dihydro-
imidazo[4,5,1-k][1,4]benzodiazepin-7(4H)-one
- 10 7. 2-(4-(2-pyrrolidin-1-yleth-1-yloxy)phenyl)-5,6-dihydroimid-
azo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
8. 2-(4-(2-piperazin-1-yleth-1-yloxy)phenyl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 15 9. 2-(4-(2-(4-methylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-
dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
10. 2-(4-(2-(4-propylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-
20 dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
11. 2-(4-(2-(4-ethylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-
dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 25 12. 2-(4-(2-(4-benzylpiperazin-1-yl)eth-1-yloxy)phenyl)-5,6-
dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
13. 2-(4-(2-(4-acetamidopiperazin-1-yl)eth-1-yloxy)phenyl)-
5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 30 14. 2-(4-(2-(4-benzamidopiperazin-1-yl)eth-1-yloxy)phenyl)-
5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
15. 2-(4-(4-methylhomopiperazin-1-yl)phenyl)-5,6-dihydroimidazo-
35 [4,5,1-jk][1,4]benzodiazepin-7(4H)-one
16. 2-(4-(4-benzylhomopiperazin-1-yl)phenyl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 40 17. 2-(4-(4-n-butylhomopiperazin-1-yl)phenyl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
18. 2-(4-(4-ethylhomopiperazin-1-yl)phenyl)-5,6-dihydroimidazo-
[4,5,1-jk][1,4]benzodiazepin-7(4H)-one

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34. 2-thien-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
35. 2-indol-5-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodi-
5 azepin-7(4H)-one
36. 2-indol-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodi-
azepin-7(4H)-one
- 10 37. 2-quinolin-3-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
38. 2-isoquinolin-1-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
- 15 39. 2-quinoxalin-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzo-
diazepin-7(4H)-one
40. 2-naphth-2-yl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodi-
20 azepin-7(4H)-one
41. 2-(2-(N,N-dimethylamino)eth-1-ylamino)phenyl)-5,6-dihydro-
imidazo[4,5,1-k][1,4]benzodiazepin-7(4H)-one
- 25 42. 2-(2-(N,N-diethylamino)eth-1-ylamino)phenyl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
43. 2-(2-piperidin-1-yleth-1-ylamino)phenyl)-5,6-dihydroimid-
azo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 30 44. 2-(2-pyrrolidin-1-yleth-1-ylamino)phenyl)-5,6-dihydroimid-
azo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
45. 2-(3-(N,N-dimethylamino)prop-1-ylamino)phenyl)-5,6-dihydro-
35 imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
46. 2-(3-(N,N-diethylamino)prop-1-ylamino)phenyl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 40 47. 2-(3-piperidin-1-ylprop-1-ylamino)phenyl)-5,6-dihydroimid-
azo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
48. 2-(3-pyrrolidin-1-ylprop-1-ylamino)phenyl)-5,6-dihydro-
imidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
- 45

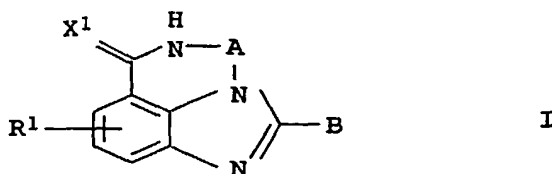
49. 2-cyclohexyl-5,6-dihydroimidazo[4,5,1-jk][1,4]benzodiazepin-7(4H)-one
50. 2-(cis-4-aminocyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-jk]-
5 [1,4]benzodiazepin-7(4H)-one
51. 2-(4-methoxycyclohex-1-yl)-5,6-dihydroimidazo[4,5,1-jk]-
[1,4]benzodiazepin-7(4H)-one
- 10 52. 2-phenyl-5,6-dihydroimidazo[5,4,1-jk][1,4]benzodiazepin-
7(4H)-one
53. 2-(3-aminophenyl)-5,6-dihydroimidazo[5,4,1-jk][1,4]benzo-
diazepin-7(4H)-one
- 15 54. 2-(4-N,N-dimethylaminomethylphenyl)-5,6-dihydroimidazo-
[5,4,1-jk][1,4]benzodiazepin-7(4H)-one
55. 2-(4-(2-N,N-dimethylaminoeth-1-yl)phenyl)-5,6-dihydro-
20 imidazo[5,4,1-jk][1,4]benzodiazepin-7(4H)-one
56. 2-(4-hydroxyphenyl)-5,6-dihydroimidazo[5,4,1-jk][1,4]benzo-
diazepin-7(4H)-one
- 25 57. 2-(4-pyrrolidinemethylphenyl)-5,6-dihydroimidazo[5,4,1-jk]-
[1,4]benzodiazepin-7(4H)-one
58. 2-(2-methylthiophenyl)-5,6-dihydroimidazo[5,4,1-jk][1,4]-
benzodiazepin-7(4H)-one
- 30 59. 2-(4-carboxyphenyl)-5,6-dihydroimidazo[5,4,1-jk][1,4]benzo-
diazepin-7(4H)-one
60. 2-(3,5-bis(trifluoromethyl)phenyl)-5,6-dihydroimidazo-
35 [5,4,1-jk][1,4]benzodiazepin-7(4H)-one
61. 2-(4-tert-butylphenyl)-5,6-dihydroimidazo[5,4,1-jk][1,4]-
benzodiazepin-7(4H)-one
- 40 62. 2-(3-(morpholin-4-ylmethyl)phenyl)-5,6-dihydroimidazo-
[5,4,1-jk][1,4]benzodiazepin-7(4H)-one

We claim:

1. A compound of the formula I

5

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in which

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A can be a C₁-C₃ chain where each carbon atom may also carry one or two of the following substituents: C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, COOH, COO-C₁-C₄-alkyl and phenyl or one C atom may also carry an =O group, and

20

X¹ can be S, O and NH, and

25

R¹ is hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C₁-C₆-alkyl, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, O-C₁-C₄-alkyl, where R¹¹ and R¹² are, independently of one another, hydrogen or C₁-C₄-alkyl, and R¹³ is hydrogen, C₁-C₄-alkyl, C₁-C₄-alkyl-phenyl or phenyl, and

30

B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by one R⁴ and a maximum of 3 different or identical R⁵ radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups, or is a radical L_v-Y-M_w in which

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L can be a straight-chain or branched, saturated or unsaturated carbon chain of 1 to 8 C atoms, it being possible for each carbon atom to be substituted by one or two R⁴ radicals and a maximum of two different or identical R⁵ radicals, and

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M has, independently of L, the same meaning as L, and

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Y is a bond, or can be S, O or NR^3 , where R^3 can be hydrogen, branched and unbranched $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_1\text{-C}_4\text{-alkyl-phenyl}$, phenyl, and

5 v can be 0 and 1, and

w can be 0 and 1, and

10 when Y is a bond, R^4 and R^5 are not both hydrogen, and

when B is $\text{L}_v\text{-Y-M}_w$, R^1 is not chlorine or NO_2 , and

R^4 is hydrogen and $-(\text{D})_p-(\text{E})_s-(\text{F}^1)_q-\text{G}^1-(\text{F}^2)_r-(\text{G}^2)-\text{G}^3$, where

15 D can be S, NR^{43} and O

E can be phenyl,

20 $\begin{array}{c} \diagup \\ \text{C}=\text{O}, \\ | \end{array}$ $-\text{SO}_2-$, $-\text{SO}_2\text{NH}-$, $-\text{NHCO}-$, $-\text{CONH}-$, NHSO_2- ,
 $-\text{NHCOCH}_2\text{X}^4$,
 and

X^4 can be S, O or NH, and

25 F^1 can be a straight-chain or branched saturated or unsaturated carbon chain of 1 to 8 C atoms, and

F^2 has, independently of F^1 , the same meaning as F^1 ,

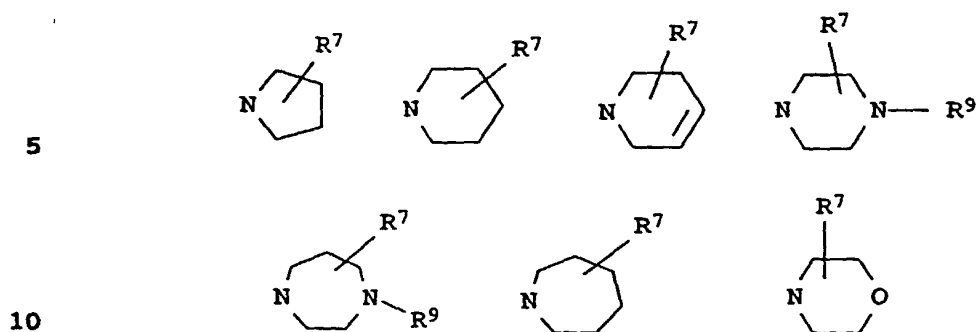
30 G^1 is a bond or can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and
 35 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R^5 radicals, and one or two carbon or sulfur atoms may also carry one or two $=\text{O}$ groups, and

40

G^2 is $\text{NR}^{41}\text{R}^{42}$ and

45

50



or a bond, and

15 G^3 can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical radicals R^5 , and one or two carbon or sulfur atoms may also carry one or two =O groups, or is hydrogen, and

20

25 p can be 0 and 1 and

s can be 0 and 1 and

30 q can be 0 and 1 and

r can be 0 and 1 and

35 R^{41} can be hydrogen, C_1 - C_6 -alkyl, it being possible for each carbon atom also to carry up to two R^6 radicals, phenyl which may also carry a maximum of two R^6 radicals, and $(CH_2)_t$ -K and

40 R^{42} can be hydrogen, C_1 - C_6 -alkyl, $-CO-R^8$, CO_2-R^8 , SO_2NH_2 , SO_2-R^8 , $-(C=NH)-R^8$ and $-(C=NH)-NHR^8$ and

R^{43} can be hydrogen and C_1 - C_4 -alkyl and

t can be 1, 2, 3, 4 and

45 K can be $NR^{11}R^{12}$, NR^{11} - C_1 - C_4 -alkyl-phenyl, pyrrolidine, piperidine, 1,2,5,6-tetrahydropyridine, morpholine, homopiperidine, piperazine, which may also be substituted

5 R⁵ can be hydrogen, chlorine, fluorine, bromine, iodine, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, C₁-C₄-alkyl-CO-NH-R¹³, COR⁸, C₀-C₄-alkyl-O-CO-R¹³, C₁-C₄-alkyl-phenyl, phenyl, CO₂-C₁-C₄-alkyl, and branched and unbranched C₁-C₆-alkyl, O-C₁-C₄-alkyl, S-C₁-C₄-alkyl, it being possible for each C atom of the alkyl chains to carry up to two R⁶ radicals, and for the alkyl chains also to be unsaturated, and,

10

15 R⁶ can be hydrogen, chlorine, fluorine, bromine, iodine, branched and unbranched C₁-C₆-alkyl, OH, nitro, CF₃, CN, NR¹¹R¹², NH-CO-R¹³, O-C₁-C₄-alkyl,

20 R⁷ can be hydrogen, C₁-C₆-alkyl, phenyl, it being possible for the ring also to be substituted by up to two R⁷¹ radicals, and an amine NR¹¹R¹² or a cyclic saturated amine which has 3 to 7 members and may also be substituted by an alkyl radical C₁-C₆-alkyl, and homopiperazine which may also be substituted by an alkyl radical C₁-C₆-alkyl,

25 and where the radicals R¹¹, R¹² and R¹³ in K, R⁵, R⁶ and R⁷ may, independently of one another, assume the same meaning as for R¹, and

30 R⁷¹ can be OH, C₁-C₆-alkyl, O-C₁-C₄-alkyl, chlorine, bromine, iodine, fluorine, CF₃, nitro, NH₂, and

35 R⁸ can be C₁-C₆-alkyl, CF₃, phenyl, C₁-C₄-alkyl-phenyl, it being possible for the ring also to be substituted by up to two R⁸¹ radicals, and

40 R⁸¹ can be OH, C₁-C₆-alkyl, O-C₁-C₄-alkyl, chlorine, bromine, iodine, fluorine, CF₃, nitro, NH₂, and

45 R⁹ can be hydrogen, C₁-C₆-alkyl, C₁-C₄-alkyl-phenyl, CO₂-C₁-C₄-alkyl-phenyl, CO₂-C₁-C₄-alkyl, SO₂-phenyl, COR⁸ and phenyl, it being possible for the phenyl rings also to be substituted by up to two R⁹¹ radicals, and

50 R⁹¹ can be OH, C₁-C₆-alkyl, O-C₁-C₄-alkyl, chlorine, bromine, iodine, fluorine, CF₃, nitro, NH₂,

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and its tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof.

2. A compound of the formula I as claimed in claim 1, where
5
A is a C₂ chain, which may be substituted, and
X¹ is O, and
10 R¹ is hydrogen.
3. A compound of the formula I as claimed in either of claims 1 or 2, in which
15 B can be an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 15 carbon atoms, an unsaturated, saturated or partially unsaturated mono-, bi- or tricyclic ring with a maximum of 14 carbon atoms and 0 to 5 nitrogen atoms, 0 to 2 oxygen atoms or 0
20 to 2 sulfur atoms, each of which may also be substituted by a maximum of 3 different or identical R⁵ radicals, and one or two carbon or sulfur atoms may also carry one or two =O groups.
- 25 4. A compound of the formula I as claimed in claim 3, where
B is phenyl, cyclohexyl, piperidine, pyridine, pyrimidine, pyrrole, pyrazole, thiophene, furan, oxazole, naphthalene, piperazine, quinoline, pyrazine, each of
30 which may also be substituted by one R⁴ or a maximum of 2 R⁵.
5. A compound of the formula I as claimed in claim 4, where
35 R⁴ is hydrogen or D_{0,1}-F¹_{0,1}-G²-G³ with G³ equal to hydrogen, and
D is O and NR⁴³, where R⁴³ is hydrogen and C₁-C₃-alkyl and
40 F¹ is C₂-C₄-alkyl.
6. A compound of the formula I as claimed in either of claims 1 or 2, in which B is L_v-Y-M_w, where
45 v is 0, and

53

- w is 1, and
- Y is a bond, and
- 5 M can be a straight-chain or branched carbon chain of 2 to 8 C atoms which contains at least one double bond, it being possible for each carbon atom to be substituted by one or two R⁴ radicals and a maximum of two different or identical R⁵ radicals, and
- 10 R¹ is hydrogen, and
- R⁴ is D_{0,1}-F¹_{0,1}-G¹-G²-G³, with G³ equal to hydrogen, and
- 15 D is O and NR⁴³, where R⁴³ is hydrogen and C₁-C₃-alkyl and
- F¹ is C₂-C₄-alkyl.
7. A drug comprising one or more compounds of the formula I as
- 20 claimed in any of claims 1 to 6 in addition to conventional carriers and excipients.
8. The use of compounds of the formula I as claimed in any of
- 25 claims 1 to 6 or of the formula I where R¹, X¹ and A have the meaning as above, and B can be hydrogen and a C₁-C₆-alkyl chain, for producing drugs with a PARP-inhibiting effect.
9. The use of compounds of the formula I as claimed in claim 8
- 30 for producing drugs for treating neurodegenerative disorders and neuronal damage.
10. The use as claimed in claim 8 for treating neurodegenerative
- disorders and neuronal damage caused by ischemia, trauma or massive bleeding.
- 35 11. The use as claimed in claim 8 for treating stroke and craniocerebral trauma.
12. The use as claimed in claim 8 for treating Alzheimer's
- 40 disease, Parkinson's disease and Huntington's disease.
13. The use of compounds of the formula I as claimed in claim 8
- for producing drugs for the treatment or prophylaxis of damage due to ischemias.

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14. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of epilepsies, in particular of generalized epileptic seizures, such as, for example, petit mal and tonoclonic seizures and partial epileptic seizures, such as temporal lobe, and complex partial seizures.
15. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the kidneys after renal ischemia, damage caused by drug therapy such as, for example, during cyclosporin therapy, and for treatment during and after kidney transplants.
16. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of damage to the heart following cardiac ischemia.
17. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of microinfarcts such as, for example, during and after heart valve replacement, aneurysm resections and heart transplants.
18. The use of compounds of the formula I as claimed in claim 8 for producing drugs for treatment in cases of revascularization of critically narrowed coronary arteries such as, for example, in PTCA and bypass operations or of critically narrowed peripheral arteries, especially leg arteries.
19. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of acute myocardial infarct and of damage during and after medical or mechanical lysis thereof.
20. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of tumors and metastasis thereof.
21. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of sepsis, of multiorgan failure such as, for example, during septic shock and of acute respiratory distress syndrome.

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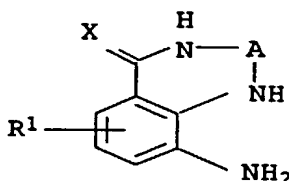
22. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of immunological disorders such as inflammations and rheumatic disorders such as, for example, rheumatoid arthritis.

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23. The use of compounds of the formula I as claimed in claim 8 for producing drugs for the treatment of diabetes mellitus.

24. A compound of the formula III

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III

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in which

20 A is a C₁-C₃ chain it being possible for each carbon atom also to carry one or two of the following substituents: C₁-C₄-alkyl, OH, O-C₁-C₄-alkyl, CO₂H, CO₂-C₁-C₄-alkyl and phenyl or one C atom may also carry an =O group, and

25 X¹ and R¹ have the meanings stated in the previous claims,

excluding the compounds

9-amino-3-methyl-1,2,3,4-tetrahydro-5H-1,4-benzodiazepin-5-one,

30 9-amino-3-methyl-3,4-dihydro-1H-1,4-benzodiazepine-2,5-dione,
6,8-diamino-2,4-(1H,3H)-quinazolinedione,
8-amino-2,4-(1H,3H)-quinazolinedione,

and the salts thereof.

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25. A process for preparing compounds of the formula III and salts thereof, wherein 2-halo-3-nitrobenzoic esters are reacted with a suitable diamine in a polar solvent in the presence of a base, and then the nitro group is hydrogenated with hydrogen in the presence of a suitable catalyst.

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26. The use of compounds of the formula III in the synthesis of PARP inhibitors.

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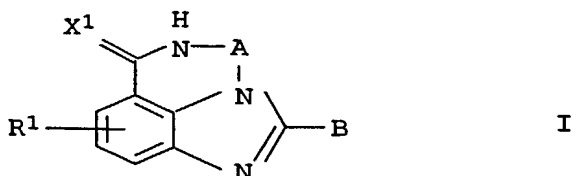
Benzodiazepine derivatives, the preparation and use thereof

Abstract

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The invention relates to compounds of the formula I

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15 and their tautomeric forms, possible enantiomeric and diastereomeric forms, and prodrugs thereof, the preparation and use thereof, where the values have the meaning stated in the description.

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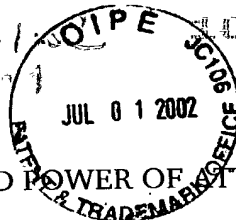
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PATENT & TRADEMARK OFFICE

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

BENZODIAZEPINE DERIVATIVES, THE PREPARATION AND USE THEREOF

the specification of which:

- ☐ is attached hereto.
☒ was filed as 10/088,604 as U.S. Application Serial No.
☒ was filed as PCT/EP00/09023 as PCT Application Serial No.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

☐ In compliance with this duty, attached is an information disclosure statement.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed	
			Yes	No
<u>199 46 289.5</u>	<u>GERMANY</u>	<u>Sept. 28, 1999</u>	<input type="checkbox"/>	<input type="checkbox"/>
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/>	<input type="checkbox"/>
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/>	<input type="checkbox"/>
<u> </u>	<u> </u>	<u> </u>	<input type="checkbox"/>	<input type="checkbox"/>
Number	Country	Date Filed		

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:


Serial No.	Date	Status
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I hereby appoint KEIL & WEINKAUF their attorneys and/or agents: Herbert B. Keil, Reg. No. 18,967; Russell E. Weinkauff, Reg. No. 18,495; Gerald H. Bjorge, Reg. No. 32,386; Norman G. Torchin, Reg. No. 34,068; Henry R. Jiles, Reg. No. 32,677; Jason D. Voight, Reg. No. 42,205; George F. Helfrich, Reg. No. 22,350; Ronald H. Smith, Reg. No. 43,679; David C. Liechty, Reg. No. 48,692, the address of all being KEIL & WEINKAUF, 1101 Connecticut Avenue, N.W., Suite 620, Washington, D.C. 20036 (telephone (202)659-0100), with full power to prosecute this application and transact all business in the Patent Office connected therewith.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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